**REMARKS**

The Office Action mailed December 17, 2004, has been received and its contents carefully noted. Claims 1, 4-15 and 17-22 are pending in the application.

**Rejection under 35 U.S.C. §103**

The Examiner rejected claims 1, 4-6, and 17-19 under 35 U.S.C. § 103(a), as being unpatentable over GB '906 in view of US 5,830,463 ('463 patent). The Examiner states that GB '906 discloses a controlled release or transdermal or oral device which read on the solid carrier of claim 5 and the patch of claim 16. The active agent is contained in a plurality of microcapsules and is nicotine. The active agent is delivered with a solvent and that the mechanism of action of the encapsulated nicotine is inherent in the prior art. The Examiner continues that GB '906 does not teach microcapsules comprising yeast cells or a mixture of yeast cells having nicotine and those without nicotine. The Examiner states further that the '463 patent teaches yeast cells for drug delivery and as such one of

ordinary skill in the art would have been motivated to combine the teaching of yeast cells of the '463 patent with the nicotine encapsulation of GB '906 to result in the claimed invention. Applicants respectfully traverse this rejection.

Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art. "The test for an implicit showing is what the combined teachings, knowledge of one of ordinary skill in the art, and the nature of the problem to be solved as a whole would have suggested to those of ordinary skill in the art." In re Kotzab, 217 F.3d 1365, 1370, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000). The combination of the GB '906 or US '463 references, does not teach or disclose all of the elements of the encapsulation technology as claimed in the present invention.

In the present invention, the Applicants have provided a novel drug delivery system comprising yeast cells that are

physically incorporated with nicotine, and use the loaded yeast cells as a form of microencapsulation of the nicotine molecule.

In the Examiner's Response to Arguments in the present Office Action, the Examiner has cited the US '463 reference as evidence that one of skill in the art would consider using yeast as a safe drug delivery vehicle. Applicants assert that the '463 patent only teaches that using yeast as a vector for generating an immune response in a mammal by incorporating genes for antigens of interest that will be expressed internally, or externally from the yeast and that it can be safely done. As such, one of skill in the art would understand that the yeast cells in US '463 can only deliver large molecular weight protein products, not organic molecules like nicotine. There is nothing in the '463 patent that teaches or suggests that yeast cells can take up a pharmacologically active organic molecule into the yeast cell, would be safe for use in people as a drug delivery device, as in the present invention.

The Examiner's argument for citing the US '463 reference is by equating "coating" with "encapsulation". The

Examiner then follows this reasoning by equating the teaching of encapsulation of nicotine (in US '334) by coating with known pharmaceutical formulations like waxes, polysaccharides, or fats, to the teaching (in US '463) of inserting a foreign gene into a living cell and then having the cell make protein from that foreign gene, or (in the present invention) of making the cells of a living organism to take up nicotine from a solution and applying the loaded cells to a human. Clearly, from any scientific viewpoint, these methods cannot be equivalent.

One of skill in the drug delivery art would not be motivated to look to the transgenic vaccine therapy arts to find an appropriate delivery vehicle for simply getting a small organic molecule into the bloodstream via oral administration. The last thing that one of skill in the art would likely want to do when looking in the prior art for a drug delivery vehicle for nicotine to aid smoking cessation, would be to use a vehicle such as a living organism, that gives an immune reaction. In fact, the whole teaching of US '463 is that the non-pathogenic yeast which they used helped stimulate both humoral and cell mediated immunity! Clearly, the US '463 reference teaches away from the

use of yeast as a safe, non-toxic, non-immunoreactive method of giving a smoker some nicotine.

Furthermore, Applicant disagrees strongly with the Examiner that the primary reference, GB '906, teaches anything but standard methods for getting neuropharmacological drugs into the blood using standard transdermal drug delivery formulations including microencapsulation with well known chemical coatings. Nowhere in GB '906 is there any mention of yeast, or any description of microencapsulation methods or processes. Further, one of skill in the art, having nicotine incorporated in a synthetic semi-permeable acetate membrane having a pore, as in the GB '906 reference, would not look to the transgenic vaccine arts to find an improved method for delivering a small organic compound to the oral cavity via incorporation into the cells of a living organism. The Applicant asserts that one of skill in the are would not be motivated to combine these references, and even if one did, the combination does not teach or suggest the claimed invention as a whole, that is, the combination does not teach or suggest a novel drug delivery system comprising yeast cells that are physically incorporated with nicotine, and the use of the

nicotine loaded yeast cells as a form of microencapsulation of the nicotine molecule to give a dose of nicotine to a patient.

It appears that the Examiner is picking and choosing elements from various references without showing a motivation in the art to do so, despite the Examiner's insistence to the contrary. The Examiner has presented no line of reasoning as to why one of skill in the art, when reviewing the art, would have found it obvious to selectively pick and choose the various elements and/or concepts of GB '906 and US '463 to arrive at the present invention.

In the present Office Action, the Examiner has only cited references that show *some* of the elements of the claimed invention in one or more combinations, without addressing the suggestion or motivation in the art to do so. See Ex parte Clapp, 227 U.S.P.Q. 972 (B.P.A.I. 1985). Moreover, the mere fact that a device or process utilizes a known scientific principle does not alone make that device or process obvious. See, *Uniroyal, Inc. v. Rudkin-Wiley Corp.*, 837 F.2d 1044, 1053, 5 USPQ2d 1434, 1440 (Fed. Cir. 1988). See also Lindemann

Maschinenfabrik GmbH v. American Hoist & Derrick Co., 730 F.2d 1452, 1462, 221 USPQ 481, 489 (Fed. Cir. 1984).

Such cherry picking of references is improper, and is typical of hindsight analysis. "An Examiner may often find every element of a claimed invention in the prior art. If identification of each claimed element in the prior art were sufficient to negate patentability, very few patents would ever issue. Furthermore, rejecting patents solely by finding prior art corollaries for the claimed elements would permit an Examiner to use the claimed invention itself as a blueprint for piecing together elements in the prior art to defeat the patentability of the claimed invention. Such an approach would be an illogical and inappropriate process by which to determine patentability." Sensonics, Inc. v. Aerosonic Corp., 81 F.3d 1566, 1570, 38 USPQ2d 1551, 1554 (Fed. Cir. 1996). See also, In re Rouffet, 149 F.3d 1350, 1357-58, 47 USPQ2d 1453, 1457 (Fed. Cir. 1998)(…To counter this potential weakness in the obviousness construct, the suggestion to combine requirement stands as a critical safeguard against hindsight analysis and rote application of the legal test for obviousness).

The Examiner's statement that "...it would have been obvious to replace the microencapsulated nicotine as taught in GB '906 with yeast cells as taught by US '463, motivated by the teaching of US '463 that the yeast cells are safe and do not cause side effects, with reasonable expectation of having a delivery system comprising encapsulated nicotine..." is fatally flawed for two reasons. First, US '463 does not teach the loading or uptake of nicotine into yeast cells, as in the claimed invention. US '463 teaches the incorporation of genes into yeast and the expression of large molecular weight proteins either internally or externally, not uptake of small organic molecules. Applicant is not incorporating the genes for the synthesis of nicotine into yeast, but the chemical compound itself.

The Examiner has not provided any evidence that the claimed product would be obvious from prior-art teachings, and reflects application of an obvious-to-try standard that is improper. See Ex parte Erlich, 3 USPQ2d 1011 (B.P.A.I. 1986). In particular, the Examiner has not provided any prior art references that show non-transfected yeast cells, like the present invention, are capable of the uptake of drugs (not in-

vivo synthesis), and/or that yeast having such drugs are useful as delivery vehicles for drug into the blood of a mammal. The Applicant recently performed a search of the literature, including the USPTO, Google, and PubMed, and could not find any reference to such application of yeast cells until that of the present invention in 2004, in a press release.

In the Examiner's Response to Arguments in the outstanding Office Action, the Examiner rebutted Applicant's statements regarding non-obviousness of the claimed invention and cited In re Keller, 642 F.2d 413; 208 USPQ 871 (CCPA 1981). The Examiner stated that Applicant did not properly attack the combination of references. Applicant respectfully disagrees.

In Keller, the applicant argued that the primary reference did not teach or suggest the use of digital timing in a pacemaker. However, in Keller, unlike the present invention, the secondary references taught all of the claimed limitations not present in the primary reference, and the CCPA upheld the rejection. That is not the case here. The deficiencies of GB '906 and US '334 are not cured by the addition of the secondary

reference of US '463. The present situation is more along the lines of Ex parte Futo,59 USPQ2D 1955 (BPAI 2000)("For the reasons set forth above, we do not agree with the Examiner that Vollers (the primary reference) discloses all of the subject matter recited in claim 1 except for the engaging surfaces in the wrench body, in that it does not disclose or teach the construction required by the final seven lines of the claim. This deficiency is not cured by further considering Moulin, Goss or Gilbert (the secondary references)").

In the present case, the Examiner's obviousness rejections appear to be based on the premise that US '463 teaches that yeast can be used to deliver any type of drug, which is not the case. US '463 only teaches that yeast can be transfected to express large molecular weight proteins which can function as vehicles for immunization of mammals. Nowhere in US '463 is there taught a way to incorporate small organic molecules into yeast, or their use as drug delivery vehicles, nor did the Examiner find any prior art evidence that one of skill in the art would have been motivated to, outside the specification of Applicant's invention. All of the limitations in the rejected

claims are not taught or suggested by the combination of GB '906 or US '334 in view of US '463.

Notwithstanding the foregoing, Applicant asserts in addition that "Evidence of secondary considerations may often be the most probative and cogent evidence in the record. It may often establish that an invention appearing to be obvious in light of the prior art was not. It is to be considered as part of all the evidence, not just when the decision maker remains in doubt after reviewing the art." In re Piasecki and Meyers, 745 F2d 1468, 223 USPQ 785, 790 (Fed. Cir. 1984). As evidence of commercial success of the claimed invention, Applicant has included a copy of a press release showing that the Assignee of the present invention (MICAP) had signed a deal with a large pharmaceutical company (Skyepharma) for rights to this yeast technology, as Exhibit A. A large drug company like Skyepharma would understand whether such technology was patentable and nonobvious, and is an excellent indicator of the nonobvious nature of the present invention.

As the combination of the GB '906 and US '463 references do not contain all of the elements of the claimed invention, in view of the foregoing examples and remarks, Applicants believe they have overcome the Examiner's rejection and respectfully request its withdrawal.

The Examiner rejected claims 1, 4-6, and 17-19 under 35 U.S.C. §103(a) as unpatentable over US '334 in view of US '463. The Examiner stated that US '334 teaches a controlled release form of nicotine using microencapsulation but does not teach use of yeast for microencapsulation, and that, as in the previous rejection, US '463 teaches yeast cells for drug delivery and are safe. The Examiner then states "...it would have been obvious to obtain a controlled release delivery system comprising encapsulated nicotine as taught by US '334 and replace the microencapsulated nicotine and excipient as taught by US '463, motivated by the teaching of US '463 that the yeast cells are safe and do not cause side effects, with reasonable expectation of having a delivery system comprising encapsulated nicotine..." Applicant respectfully traverses this rejection.

First, as stated in the reasons set forth in regards to the previous rejection, Applicant asserts that US '463 does not teach the loading or uptake of nicotine into yeast cells, as in the claimed invention. US '463 teaches the incorporation of genes into yeast and the expression of large molecular weight proteins either internally or externally, not uptake of small organic molecules. Applicant is not incorporating the genes for the synthesis of nicotine into yeast, but the chemical compound itself.

US '334 teaches a lollipop device which can have nicotine microencapsulated using fats waxes, triglycerides and other materials.

In addition to motivation, in order to establish *prima facie* obviousness of a claimed invention, *all* the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). The Applicant submits that, even if motivation could be shown to exist in the art, the combination of US '334 and US '463 does not teach or suggest all of the claim elements of the rejected claims of the

present invention. The combination fails to teach all the elements of claim 1, a delivery system for nicotine comprising nicotine microencapsulated in yeast wherein the nicotine is released on contact with the buccal cavity, because the combination fails to include the element of nicotine containing yeast cells as the form of microencapsulated nicotine as taught in US '334. Yeast cells in US '463 that can express proteins of interest, do not teach or suggest yeast cells made to take up and deliver small organic molecules like nicotine. Furthermore, with regard to claims 17-19, none of the references cited contain the limitation of yeast cells having a loading of nicotine of about 25 to 60% by weight. As such, the Examiner has failed to make a prima facie case of obviousness and the Applicant requests withdrawal of this rejection.

The Examiner rejected claims 6-9, 12-15, 20 and 21 under 35 U.S.C. §103(a) as unpatentable over GB '906 in view of US '463 and further in view of US 5,733,574 (US '574).

The Examiner states, *inter alia*, that it would have been obvious to combine the controlled delivery system of GB '906

in the form of a lozenge and flavoring agents as disclosed by US '574, motivated by the teaching of US '574 that delivery units in the form of a lozenge provide nicotine dose corresponding to the stimulation of nicotine obtained by smoking a cigarette. Applicants respectfully traverse this rejection.

For the reasons already made of record above, Applicant asserts that the combination of GB '906, US '574 and US '463 does not teach or suggest all of the claim elements of the rejected claims of the present invention. In particular, as asserted above, yeast cells as taught in US '463 can express proteins of interest, but US '463 does not teach or suggest yeast cells made to take up and deliver small organic molecules like nicotine. Moreover, they do not teach yeast cells having a loading of nicotine of about 25 to 60% by weight. As such the combination of references also does not teach or suggest all the claim limitations and Applicant respectfully requests withdrawal of this rejection.

The Examiner rejected claims 10 and 22 under 35 U.S.C. §103(a) as unpatentable over GB '906 in view of US '463 and US

'574 as applied to the previous rejection and further in view of US '060 and GB 2 299 756 (GB '756).

The Examiner states that claims 10 and 22 recite a lozenge having 5-20 cm in length and preferred snapping positions. The GB '906, US '463 and US '574 references do not teach such a lozenge, however GB '756 teaches a product in the form of a pastille for oral ingestion having nicotine and a flavoring agent, being capable of delivering a quantity of nicotine equivalent to smoking a cigarette and that the product is in the form of a rod or bar and has zones of weakness to allow it to be broken into smaller pieces. As such the Examiner asserts that it would have been obvious to one of skill in the art to deliver the delivery system in the form of a lozenge as taught by GB '906 in view of any of US '574 or US '060 and select the bar like shape of GB '756 and that one would have been motivated to do so. Applicants traverse this rejection.

For the reasons already made of record above, Applicant asserts that the combination of GB '906, US '574 and US '463 in view of GB '756 does not teach or suggest all of the claim

elements of the rejected claims of the present invention. In particular, as asserted above, yeast cells as taught in US '463 can express proteins of interest, but US '463 does not teach or suggest yeast cells made to take up and deliver small organic molecules like nicotine. Moreover, with regard to claim 22, they do not teach yeast cells having a loading of nicotine of about 25 to 60% by weight. As such the combination of references also does not teach or suggest all the claim limitations in claims 10 and 22, and Applicant respectfully requests withdrawal of this rejection.

Applicants believe that all rejections have been properly overcome and the claims as amended are in condition for allowance.

If there are any questions, the Examiner is invited to call the undersigned attorney at 202-638-6666. Entry of the amendment and reconsideration is respectfully requested.

Respectfully submitted,

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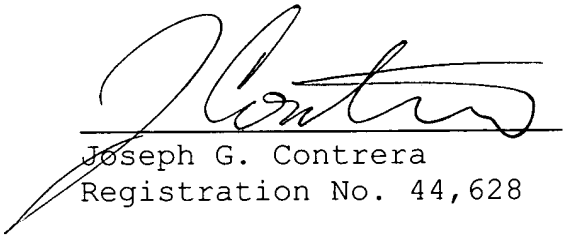

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